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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/030,585	05/22/2002	John R. Riordan	07039-167002	5671

7590 09/02/2005

Fish & Richardson
60 South Sixth Street Suite 3300
Minneapolis, MN 55402

EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 09/02/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/030,585	RIORDAN ET AL.	
	Examiner	Art Unit	
	Joseph F. Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 July 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 5-53* is/are pending in the application.

4a) Of the above claim(s) *9-50* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3, 5-8, 51-53* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *03012004;01082002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Sequence Comparison A-D*.

5.00

DETAILED ACTION

Election/Restrictions

Claims 1-3, 5-53 are pending. Claims 9-50 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 07/5/2005. Claims 1-3, 5-8, 51-53 are under consideration.

Claim Rejections - 35 USC § 112 first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 7, 51-53 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to polypeptides comprising variant sequences, and polynucleotides encoding these polypeptides. Claims 1-2, 7, 51-52 are not enabled since insufficient guidance is provided as to the function of the myriad of polypeptides and encoding nucleic acids. In addition, the claims are drawn to isolated polypeptides with a defined sequence, however, no function is provided for the polypeptides. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible variants of the polypeptides. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. As an

example of the unpredictable effects of mutations on protein function, Mickle et al. teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR) (page 597). Several mutations can cause CF, including the G551D mutation. In this mutation a glycine replaces the aspartic acid at position 551, giving rise to the CF phenotype. In the most common CF mutation, delta-F508, a single phenylalanine is deleted at position 508, giving ride to the CF phenotype. Thus showing that even the substitution or deletion of a single amino acid in the entire 1480 amino acid CFTR protein sequence can have dramatic and unpredictable effects on the function of the protein. Additionally, it is known in the art that even a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). Additionally, Yan et al. teaches that in certain cases, a change of two-amino acid residues in a protein results in switching the binding of the protein from one receptor to another (Yan et al., Two-amino acid molecular switch in an epithelial morphogen that regulates binding to two distinct receptors. *Science* 290: 523-527, 2000). Since the claims encompass nucleic acids encoding variant polypeptides and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of

enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. The claims do not set forth a functional limitation for the encoding nucleic acids or variant polypeptides and since the amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polynucleotides and encoded polypeptides for which no function is set forth.

In addition, claim 53 is not enabled because Applicants have provided no guidance or working examples of any methods of treatment for any diseases using these polypeptides, including any data or treatment regimen. Furthermore, it is not predictable to one of ordinary skill in the art how to use a pharmaceutical composition. Applicants can overcome this rejection by amending the claims to recite the proteins which are "in a pharmaceutically acceptable carrier."

Claim 5 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated CFTR polypeptide with a mutant arginine with an enhanced export, does not reasonably provide enablement for any other isolated polypeptide with a mutant arginine with an enhanced export function. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The claims are drawn to a polypeptide comprising a mutation in an R-X-R sequence, wherein the mutant has an enhanced export relative to the non-mutant form. Applicant has only provided examples using CFTR. Applicants do not disclose any actual or prophetic examples on expected performance parameters of any of the possible variants in polypeptides other than CFTR. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. As an example of the unpredictable effects of mutations on protein function, Mickle et al. teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR) (page 597). Several mutations can cause CF, including the G551D mutation. In this mutation a glycine replaces the aspartic acid at position 551, giving rise to the CF phenotype. In the most common CF mutation, delta-F508, a single phenylalanine is deleted at position 508, giving ride to the CF phenotype. Thus showing that even the substitution or deletion of a single amino acid in the entire 1480 amino acid CFTR protein sequence can have dramatic and unpredictable effects on the function of the protein. Additionally, it is known in the art that even a single amino acid change in a protein's sequence can drastically affect the structure of the protein and the

architecture of an entire cell. For example, Voet et al. (1990) teaches that a single Glu to Val substitution in the beta subunit of hemoglobin causes the hemoglobin molecules to associate with one another in such a manner that, in homozygous individuals, erythrocytes are altered from their normal discoid shape and assume the sickle shape characteristic of sickle-cell anemia, causing hemolytic anemia and blood flow blockages (pages 126-128, section 6-3A and page 230, column 2, first paragraph). Additionally, Yan et al. teaches that in certain cases, a change of two-amino acid residues in a protein results in switching the binding of the protein from one receptor to another (Yan et al., Two-amino acid molecular switch in an epithelial morphogen that regulates binding to two distinct receptors. *Science* 290: 523-527, 2000). Since the claims encompass nucleic acids encoding variant polypeptides and given the art recognized unpredictability of the effect of mutations on protein function, it would require undue experimentation to make and use the claimed invention. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue, since the amino acid sequence of a polypeptide determines its structural and functional properties, and the predictability of which amino acids can be substituted is extremely complex and outside the realm of routine experimentation, because accurate predictions of a polypeptide's structure from mere sequence data are limited. Since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polynucleotides and polypeptides that the specification only teaches one skilled in the art to test for functional variants. Since the claims

do not enable one of skill in the art to make and use the claimed polypeptides, but only teaches how to screen for the claimed polypeptides, and since detailed information regarding the structural and functional requirements of the polynucleotide and the encoded polypeptide are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims.

Claims 1-2, 5-7, 51-52 are rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

The claims are drawn to polypeptides comprising variant sequences, and polynucleotides encoding these polypeptides. Claims 1-2, 5-7, 51-52 are not described since insufficient guidance is provided as to the function of the myriad of polypeptides and encoding nucleic acids. In addition, the claims are drawn to isolated polypeptides with a defined sequence, however, no function is provided for the polypeptides. In addition, claims 5-6 are directed to a polypeptide comprising a mutation in an R-X-R sequence, wherein the mutant has an enhanced export relative to the non-mutant form. The specification and claims do not place any limit on the number of amino acid substitutions, deletions, insertions and/or additions that may be made to the encoded variants. Thus, the scope of the claim includes numerous structural variants, and the

genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the nucleic acid class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, the genus is insufficiently described. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus of polynucleotides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polynucleotides and polypeptides encompassed. Thus, no identifying characteristics or properties of the instant polypeptides are provided such that one of skill would

be able to predictably identify the encompassed molecules as being identical to those instantly claimed. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 7, 51-52 are rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent Number 5, 639,661 (Welsh et al.).

The claims are drawn to an isolated polypeptide comprising a polypeptide having the sequence X-R-X-R-X, and polynucleotides encoding them. Claims 1-3 are anticipated because the '661 patent discloses a polypeptide comprising the sequences of SEQ ID NO: 1-4 (See Sequence Comparisons A-D, attached). Claims 7, 51-52 are anticipated because the '661 patent discloses encoding polynucleotides (see Column 4, lines 25-30).

Claim 8 is rejected under 35 U.S.C. 102(b) as being anticipated by U.S. Patent No. 5,750,571 (Cheng et al.).

The claim is drawn to a method of identifying a therapeutic agent which increases the amount of export-incompetent CFTR which reaches the cell membrane. The claim is anticipated because the '571 patent discloses the treatment of cystic fibrosis-associated (CF-associated) cells

with butyrate resulted in functional mutant cystic fibrosis transmembrane regulator (CFTR) protein within the CF-associated cells. The butyrate facilitated the delivery of the mutant CFTR to the appropriate location within the CF-associated cell (the plasma membrane) and the mutant CFTR of butyrate-treated cells was capable of generating chloride channels (column 2, lines 25-35).

References

The Office will no longer be supplying paper copies of U.S. Patents cited in Office Actions. Applicant is advised that the cited U.S. patents and patent application publications are available for download via the Office's PAIR. As an alternate source, all U.S. patents and patent application publications are available on the USPTO web site (www.uspto.gov), from the Office of Public Records and from commercial sources. Applicant may direct inquiries about the use of the Office's PAIR system to the Electronic Business Center (EBC) at http://www.uspto.gov/ebc/index.html or 1-866-217-9197.

Conclusion

Claims 1-3, 5, 7-8, 51-53 are rejected.

Claim 6 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Murphy whose telephone number is (571) 272-0877. The examiner can normally be reached Monday through Friday from 7:30 am to 5:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (571) 272-0829.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Joseph F. Murphy, Ph. D.
Primary Examiner
Art Unit 1646
August 29, 2005

JOSEPH MURPHY
PATENT EXAMINER

Sequence Comparison A
SEQ ID NO: 1

```
RESULT 1
US-08-216-971-2
; Sequence 2, Application US/08216971
; Patent No. 5639661
;  GENERAL INFORMATION:
;    APPLICANT:  Welsh, Michael J.
;    APPLICANT:  Sheppard, David N.
;    TITLE OF INVENTION:  NOVEL GENES AND PROTEINS FOR TREATING
;    TITLE OF INVENTION:  CYSTIC FIBROSIS
;    NUMBER OF SEQUENCES:  2
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  LAHIVE & COCKFIELD
;      STREET:  60 State Street, suite #510
;      CITY:  Boston
;      STATE:  Massachusetts
;      COUNTRY:  USA
;      ZIP:  02109-1875
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/216,971
;      FILING DATE:  23-MAR-1994
;      CLASSIFICATION:  514
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Arnold, Beth E.
;      REGISTRATION NUMBER:  35,430
;      REFERENCE/DOCKET NUMBER:  UIZ-011
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (617) 227-7400
;      TELEFAX:  (617) 227-5941
;  INFORMATION FOR SEQ ID NO:  2:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  836 amino acids
;      TYPE:  amino acid
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
US-08-216-971-2

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Qy          1 GYRQRLE 7
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Db         27 GYRQRLE 33
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Sequence Comparison B
SEQ ID NO: 2

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RESULT 8
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; Sequence 2, Application US/08216971
; Patent No. 5639661
;  GENERAL INFORMATION:
;    APPLICANT:  Welsh, Michael J.
;    APPLICANT:  Sheppard, David N.
;    TITLE OF INVENTION:  NOVEL GENES AND PROTEINS FOR TREATING
;    TITLE OF INVENTION:  CYSTIC FIBROSIS
;    NUMBER OF SEQUENCES:  2
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  LAHIVE & COCKFIELD
;      STREET:  60 State Street, suite #510
;      CITY:  Boston
;      STATE:  Massachusetts
;      COUNTRY:  USA
;      ZIP:  02109-1875
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/216,971
;      FILING DATE:  23-MAR-1994
;      CLASSIFICATION:  514
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Arnold, Beth E.
;      REGISTRATION NUMBER:  35,430
;      REFERENCE/DOCKET NUMBER:  UIZ-011
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (617) 227-7400
;      TELEFAX:  (617) 227-5941
;  INFORMATION FOR SEQ ID NO:  2:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  836 amino acids
;      TYPE:  amino acid
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
US-08-216-971-2

  Query Match             100.0%;  Score 37;  DB 1;  Length 836;
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  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 EYRYRSV 7
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Db        514 EYRYRSV 520
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Sequence Comparison C
SEQ ID NO: 3

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RESULT 7
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; Sequence 2, Application US/08216971
; Patent No. 5639661
;  GENERAL INFORMATION: '
;    APPLICANT:  Welsh, Michael J.
;    APPLICANT:  Sheppard, David N.
;    TITLE OF INVENTION:  NOVEL GENES AND PROTEINS FOR TREATING
;    TITLE OF INVENTION:  CYSTIC FIBROSIS
;    NUMBER OF SEQUENCES:  2
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  LAHIVE & COCKFIELD
;      STREET:  60 State Street, suite #510
;      CITY:  Boston
;      STATE:  Massachusetts
;      COUNTRY:  USA
;      ZIP:  02109-1875
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/216,971
;      FILING DATE:  23-MAR-1994
;      CLASSIFICATION:  514
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Arnold, Beth E.
;      REGISTRATION NUMBER:  35,430
;      REFERENCE/DOCKET NUMBER:  UIZ-011
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (617) 227-7400
;      TELEFAX:  (617) 227-5941
;  INFORMATION FOR SEQ ID NO:  2:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  836 amino acids
;      TYPE:  amino acid
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
US-08-216-971-2

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SEQ ID NO: 4

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; Sequence 2, Application US/08216971
; Patent No. 5639661
;  GENERAL INFORMATION:
;    APPLICANT:  Welsh, Michael J.
;    APPLICANT:  Sheppard, David N.
;    TITLE OF INVENTION:  NOVEL GENES AND PROTEINS FOR TREATING
;    TITLE OF INVENTION:  CYSTIC FIBROSIS
;    NUMBER OF SEQUENCES:  2
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  LAHIVE & COCKFIELD
;      STREET:  60 State Street, suite #510
;      CITY:  Boston
;      STATE:  Massachusetts
;      COUNTRY:  USA
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;    COMPUTER READABLE FORM:
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;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/216,971
;      FILING DATE:  23-MAR-1994
;      CLASSIFICATION:  514
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Arnold, Beth E.
;      REGISTRATION NUMBER:  35,430
;      REFERENCE/DOCKET NUMBER:  UIZ-011
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (617) 227-7400
;      TELEFAX:  (617) 227-5941
;  INFORMATION FOR SEQ ID NO:  2:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  836 amino acids
;      TYPE:  amino acid
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
US-08-216-971-2

  Query Match             100.0%;  Score 33;  DB 1;  Length 836;
  Best Local Similarity   100.0%;  Pred. No. 67;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 QARRRQS 7
              |||||||
Db        762 QARRRQS 768
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10030585 Results

SEQ ID NO: 1

10030585 Results:

SEQ ID NO: 1

SUMMARIES

Result No.	Score	% Query Match	Length	DB	ID	Description
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2	37	100.0	25	4	AAB31719	Aab31719 Arginine-
3	37	100.0	151	2	AAR13304	Aar13304 CFTR 556
4	37	100.0	354	6	ABR83574	Abr83574 Human CFT
5	37	100.0	492	2	AAR13236	Aar13236 CFTR Q493
6	37	100.0	541	2	AAR13296	Aar13296 CFTR G542
7	37	100.0	836	2	AAR79835	Aar79835 Truncated
8	37	100.0	1091	2	AAR13303	Aar13303 CFTR Y109
9	37	100.0	1190	2	AAR13308	Aar13308 CFTR 3659
10	37	100.0	1248	8	ABO84493	Abo84493 Human can
11	37	100.0	1461	8	ADO28621	Ado28621 Human chl
12	37	100.0	1476	2	AAY33968	Aay33968 CFTR prot
13	37	100.0	1479	2	AAR13231	Aar13231 CFTR delt
14	37	100.0	1479	2	AAR11602	Aar11602 Mutant cy
15	37	100.0	1479	2	AAY02279	Aay02279 DeltaF508
16	37	100.0	1479	5	AAU74516	Aau74516 Human del
17	37	100.0	1479	7	ADA37387	Ada37387 Human CFT
18	37	100.0	1480	2	AAR13300	Aar13300 CFTR Y563
19	37	100.0	1480	2	AAR13232	Aar13232 CFTR G85E
20	37	100.0	1480	2	AAR13234	Aar13234 CFTR G178
21	37	100.0	1480	2	AAR13233	Aar13233 CFTR I148
22	37	100.0	1480	2	AAR13235	Aar13235 CFTR A455
23	37	100.0	1480	2	AAR13298	Aar13298 CFTR G551
24	37	100.0	1480	2	AAR13302	Aar13302 CFTR L107
25	37	100.0	1480	2	AAR13301	Aar13301 CFTR P574
26	37	100.0	1480	2	AAR13299	Aar13299 CFTR R560
27	37	100.0	1480	2	AAR13297	Aar13297 CFTR S549
28	37	100.0	1480	2	AAR11115	Aar11115 Cystic fi
29	37	100.0	1480	2	AAR13894	Aar13894 Cystic fi
30	37	100.0	1480	2	AAR22492	Aar22492 Cystic Fi
31	37	100.0	1480	2	AAW68012	Aaw68012 Human cys
32	37	100.0	1480	2	AAR23074	Aar23074 Cystic fi
33	37	100.0	1480	2	AAR79011	Aar79011 CFTR enco
34	37	100.0	1480	2	AAR71095	Aar71095 Antibody
35	37	100.0	1480	2	AAR72852	Aar72852 CFTCR. 11
36	37	100.0	1480	2	AAR72384	Aar72384 Cystic fi
37	37	100.0	1480	2	AAY49869	Aay49869 Human cys
38	37	100.0	1480	2	AAY02280	Aay02280 G551D cys
39	37	100.0	1480	2	AAY02278	Aay02278 A cystic
40	37	100.0	1480	2	AAW97573	Aaw97573 Cystic fi
41	37	100.0	1480	4	AAB68049	Aab68049 A cystic
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RESULT 3
AAR13304
ID AAR13304 standard; protein; 151 AA.
XX
AC AAR13304;
XX
DT 14-OCT-1991 (first entry)

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XX
DE   CFTR 556 del A.
XX
KW   Deletion; mutant; diagnosis; antibodies; drug therapy.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
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FT                   /label= phosphorylation_site
FT                   /note= "by protein kinases C"
FT   Modified-site   63
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FT   Domain          118. .138
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PN   WO9110734-A.
XX
PD   25-JUL-1991.
XX
PF   12-JAN-1990;   90CA-02007699.
XX
PR   12-JAN-1990;   90CA-02007699.
PR   01-MAR-1990;   90CA-02011253.
PR   10-JUL-1990;   90CA-02020817.
XX
PA   (HSCR-) HSC RES DEV CORP.
XX
PI   Tsui LC,  Rommens JM,  Kerem B;
XX
DR   WPI; 1991-238022/32.
DR   N-PSDB; AAQ13068.
XX
PT   Mutant cystic fibrosis trans-membrane conductance regulator gene - used
PT   for producing prods. for diagnosis, screening and therapy of cystic
PT   fibrosis.
XX
PS   Claim 20; Page 124; 178pp; English.
XX
CC   556 del A is a frameshift mutation in exon 4 and results in shortened
CC   polypeptides significantly different from the single amino acid deletions
CC   or alterations. The mutant CF gene when expressed in cells of the human
CC   body, is associated with altered cell function which correlates with the
CC   genetic disease cystic fibrosis. See also AAQ13053-72
XX
SQ   Sequence 151 AA;

  Query Match             100.0%;  Score 37;  DB 2;  Length 151;
  Best Local Similarity   100.0%;  Pred. No. 10;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 GYRQRLE 7
              |||||||
Db         27 GYRQRLE 33


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ID   AAR13236 standard; protein; 492 AA.
XX
AC   AAR13236;
XX
DT   14-OCT-1991  (first entry)
XX
DE   CFTR Q493X.
XX
KW   Deletion; mutant; diagnosis; antibodies; drug therapy.
XX
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OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
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FT   Domain          81. .102
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FT                   /note= "by protein kinases C"
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FT   Modified-site   296
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PN   WO9110734-A.
XX
PD   25-JUL-1991.
XX
PF   12-JAN-1990;   90CA-02007699.
XX
PR   12-JAN-1990;   90CA-02007699.
PR   01-MAR-1990;   90CA-02011253.
PR   10-JUL-1990;   90CA-02020817.
XX
PA   (HSCR-) HSC RES DEV CORP.
XX
PI   Tsui LC,  Rommens JM,  Kerem B;
XX
DR   WPI; 1991-238022/32.
DR   N-PSDB; AAQ13058.
XX
PT   Mutant cystic fibrosis trans-membrane conductance regulator gene - used
PT   for producing prods. for diagnosis, screening and therapy of cystic
PT   fibrosis.
XX
PS   Claim 20; Page 124; 178pp; English.
XX
CC   In the Q493X mutation Gln (CAG) is changed into a stop codon, resulting
CC   in a shortened polypeptide significantly different from the single amino
CC   acid deletions or alterations. The mutant CF gene when expressed in cells
```

CC of the human body, is associated with altered cell function which
CC correlates with the genetic disease cystic fibrosis. See also AAQ13053-72
XX
SQ Sequence 492 AA;

Query Match 100.0%; Score 37; DB 2; Length 492;
Best Local Similarity 100.0%; Pred. No. 34;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

Qy 1 GYRQRLE 7
|||||||
Db 27 GYRQRLE 33

RESULT 7
AAR79835
ID AAR79835 standard; protein; 836 AA.
XX
AC AAR79835;
XX
DT 25-MAR-2003 (revised)
DT 02-MAY-1996 (first entry)
XX
DE Truncated cystic fibrosis transmembrane conductance regulator.
XX
KW Cystic fibrosis; transmembrane conductance; N-terminal; soluble;
KW truncated; chloride ion channel; gene therapy; CFTR; regulator;
KW epithelial cells; anion; recombinant production.
XX
OS Homo sapiens.
XX
PN WO9525796-A1.
XX
PD 28-SEP-1995.
XX
PF 23-MAR-1995; 95WO-US003680.
XX
PR 23-MAR-1994; 94US-00216971.
XX
PA (IOWA) UNIV IOWA STATE RES FOUND INC.
XX
PI Welsh MJ, Sheppard DM;
XX
DR WPI; 1995-344617/44.
DR N-PSDB; AAT04005.
XX
PT New truncated CFTR polypeptide - functions as a regulated epithelial cell
PT anion channel, used for treating cystic fibrosis.
XX
PS Claim 17; Page 70-73; 85pp; English.
XX
CC AAT04005 encodes AAR79835 a truncated N-terminal portion of the cystic
CC fibrosis transmembrane conductance regulator (CFTR), which can be used to
CC regulate the opening and closing of epithelial cell anion (chloride ion)
CC channels. The truncated cDNA is useful in CF gene therapy, as it is more
CC readily accommodated by available gene therapy vectors, and more easily
CC expressed than full length CFTR. The expressed truncated CFTR protein may
CC be more soluble and therefore more readily purified from host cells,
CC useful in the recombinant prodn. of CFTR. (Updated on 25-MAR-2003 to
CC correct PI field.)
XX
SQ Sequence 836 AA;

Query Match 100.0%; Score 37; DB 2; Length 836;
Best Local Similarity 100.0%; Pred. No. 60;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Db 27 GYRQRLE 33

SUMMARIES

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2	37	100.0	836	2	US-08-812-979-2	Sequence 2, Appli
3	37	100.0	1476	3	US-09-256-703-2	Sequence 2, Appli
4	37	100.0	1479	2	US-08-951-912-4	Sequence 4, Appli
5	37	100.0	1479	3	US-09-174-077-4	Sequence 4, Appli
6	37	100.0	1480	1	US-07-637-621-2	Sequence 2, Appli
7	37	100.0	1480	1	US-08-136-742A-2	Sequence 2, Appli
8	37	100.0	1480	1	US-08-135-809A-2	Sequence 2, Appli
9	37	100.0	1480	1	US-08-466-886-17	Sequence 17, Appl
10	37	100.0	1480	2	US-08-951-912-2	Sequence 2, Appli
11	37	100.0	1480	2	US-08-951-912-6	Sequence 6, Appli
12	37	100.0	1480	2	US-08-469-461-2	Sequence 2, Appli
13	37	100.0	1480	2	US-08-469-461-4	Sequence 4, Appli
14	37	100.0	1480	2	US-08-691-605-2	Sequence 2, Appli
15	37	100.0	1480	2	US-08-455-552A-14	Sequence 14, Appl
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17	37	100.0	1480	3	US-07-890-609-4	Sequence 4, Appli
18	37	100.0	1480	3	US-09-248-026-2	Sequence 2, Appli
19	37	100.0	1480	3	US-08-469-617-17	Sequence 17, Appl
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21	37	100.0	1480	3	US-08-681-838A-3	Sequence 3, Appli
22	37	100.0	1480	3	US-09-174-077-2	Sequence 2, Appli
23	37	100.0	1480	3	US-09-174-077-6	Sequence 6, Appli
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25	37	100.0	1480	4	US-09-425-453A-4	Sequence 4, Appli
26	37	100.0	1480	4	US-09-425-453A-6	Sequence 6, Appli
27	37	100.0	1480	4	US-09-425-453A-8	Sequence 8, Appli
28	37	100.0	1480	4	US-09-425-453A-10	Sequence 10, Appl
29	37	100.0	1480	4	US-09-425-453A-12	Sequence 12, Appl
30	37	100.0	1480	4	US-09-425-453A-14	Sequence 14, Appl
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32	37	100.0	1480	4	US-09-425-453A-18	Sequence 18, Appl
33	37	100.0	1480	4	US-09-425-453A-20	Sequence 20, Appl
34	37	100.0	1480	4	US-08-469-630-17	Sequence 17, Appl
35	37	100.0	1480	4	US-09-949-016-5949	Sequence 5949, Ap
36	37	100.0	1480	4	US-09-405-735-2	Sequence 2, Appli
37	37	100.0	1480	5	PCT-US93-11667-2	Sequence 2, Appli
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RESULT 1
US-08-216-971-2
; Sequence 2, Application US/08216971
; Patent No. 5639661
;  GENERAL INFORMATION:
;    APPLICANT:  Welsh, Michael J.
;    APPLICANT:  Sheppard, David N.
;    TITLE OF INVENTION:  NOVEL GENES AND PROTEINS FOR TREATING
;    TITLE OF INVENTION:  CYSTIC FIBROSIS
;    NUMBER OF SEQUENCES:  2
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  LAHIVE & COCKFIELD
;      STREET:  60 State Street, suite #510
;      CITY:  Boston
;      STATE:  Massachusetts
;      COUNTRY:  USA
;      ZIP:  02109-1875
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
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;       COMPUTER:  IBM PC compatible
;       OPERATING SYSTEM:  PC-DOS/MS-DOS
;       SOFTWARE:  PatentIn Release #1.0, Version #1.25
;     CURRENT APPLICATION DATA:
;       APPLICATION NUMBER:  US/08/216,971
;       FILING DATE:  23-MAR-1994
;       CLASSIFICATION:  514
;     ATTORNEY/AGENT INFORMATION:
;       NAME:  Arnold, Beth E.
;       REGISTRATION NUMBER:  35,430
;       REFERENCE/DOCKET NUMBER:  UIZ-011
;     TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  (617) 227-7400
;       TELEFAX:  (617) 227-5941
;   INFORMATION FOR SEQ ID NO:  2:
;     SEQUENCE CHARACTERISTICS:
;       LENGTH:  836 amino acids
;       TYPE:  amino acid
;       TOPOLOGY:  linear
;     MOLECULE TYPE:  protein
US-08-216-971-2

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Qy          1 GYRQRLE 7
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Db         27 GYRQRLE 33


RESULT 6
US-07-637-621-2
; Sequence 2, Application US/07637621
; Patent No. 5407796
;  GENERAL INFORMATION:
;    APPLICANT:  cutting, gary
;    APPLICANT:  antonarakis, stylianos e
;    APPLICANT:  kazazian jr., haig h
;    TITLE OF INVENTION:  CYSTIC FIBROSIS MUTATION CLUSTER
;    NUMBER OF SEQUENCES:  4
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Banner, Birch, McKie and Beckett
;      STREET:  1001 G Street, N.W.
;      CITY:  Washington, D.C.
;      COUNTRY:  USA
;      ZIP:  20001
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/07/637,621
;      FILING DATE:  19910104
;      CLASSIFICATION:  435
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  kagan, sarah a
;      REGISTRATION NUMBER:  32,141
;      REFERENCE/DOCKET NUMBER:  1107.030010
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  202-508-9100
;      TELEFAX:  202-508-9100
;  INFORMATION FOR SEQ ID NO:  2:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  1480 amino acids
;      TYPE:  AMINO ACID
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
;    ORIGINAL SOURCE:
;      ORGANISM:  HOMO SAPIENS
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US-07-637-621-2

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Best Local Similarity 100.0%; Pred. No. 25;
Matches 7; Conservative 0; Mismatches 0; Indels 0; Gaps 0;

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Db         27 GYRQRLE 33
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SEQ ID NO: 2

UMMARIES

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3	37	100.0	25	4	AAB81911	Aab81911 Human cys
4	37	100.0	26	4	AAB81910	Aab81910 Human nor
5	37	100.0	31	2	AAR97848	Aar97848 Cystic fi
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18	37	100.0	612	6	ABU37543	Abu37543 Protein e
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23	37	100.0	1279	2	AAR60873	Aar60873 STE6-CFTR
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26	37	100.0	1476	2	AAY33968	Aay33968 CFTR prot
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29	37	100.0	1479	2	AAY02279	Aay02279 DeltaF508
30	37	100.0	1479	5	AAU74516	Aau74516 Human del
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36	37	100.0	1480	2	AAR13235	Aar13235 CFTR A455
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40	37	100.0	1480	2	AAR13299	Aar13299 CFTR R560
41	37	100.0	1480	2	AAR13297	Aar13297 CFTR S549
42	37	100.0	1480	2	AAR11115	Aar11115 Cystic fi
43	37	100.0	1480	2	AAR13894	Aar13894 Cystic fi
44	37	100.0	1480	2	AAR22492	Aar22492 Cystic Fi
45	37	100.0	1480	2	AAW68012	Aaw68012 Human cys

RESULT 5
AAR97848
ID   AAR97848 standard; protein; 31 AA.
XX
AC   AAR97848;
XX
DT   07-NOV-1996 (first entry)
XX
DE   Cystic fibrosis transmembrane regulator polypeptide.
XX
KW   Cystic fibrosis; cystic fibrosis transmembrane regulator; CFTR;
KW   identification; screening; chloride; chlorine; conductance channel;
KW   pulmonary disease.
XX
OS   Synthetic.
XX
PN   WO9616084-A2.
XX
PD   30-MAY-1996.
XX
PF   06-NOV-1995;   95WO-US014345.
XX
PR   22-NOV-1994;   94US-00343714.
XX
PA   (USSH) US DEPT HEALTH & HUMAN SERVICES.
XX
PI   Pollard HB, Jacobson KA;
XX
DR   WPI; 1996-268533/27.
DR   N-PSDB; AAT30713.
XX
PT   New CFTR polypeptide(s) - used for identifying CFTR-binding cpds. partic.
PT   novel xanthine derivs., which can be used to treat cystic fibrosis.
XX
PS   Claim 1; Page 44; 61pp; English.
XX
CC   This polypeptide comprises a portion of the cystic fibrosis transmembrane
CC   regulator (CFTR) protein and may be used to identify CFTR binding
CC   compounds and compounds that can activate an impaired chlorine
CC   conductance channel in cells having a reduced apical chlorine
CC   conductance, such as cystic fibrosis. The compounds identified can also
CC   be used for treating other chronic obstructive pulmonary diseases. The
CC   polypeptide spans amino acids 509-539 of the CFTR protein
XX
SQ   Sequence 31 AA;

  Query Match   100.0%; Score 37; DB 2; Length 31;
  Best Local Similarity   100.0%; Pred. No. 1.8;
  Matches   7; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

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Db   6 EYRYRSV 12

RESULT 6
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ID   AAR97849 standard; protein; 32 AA.
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AC   AAR97849;
XX
DT   07-NOV-1996 (first entry)
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DE   Cystic fibrosis transmembrane regulator polypeptide.
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KW   Cystic fibrosis; cystic fibrosis transmembrane regulator; CFTR;
KW   identification; screening; chloride; chlorine; conductance channel;
KW   pulmonary disease.
XX
OS   Synthetic.
XX

PN   WO9616084-A2.
XX
PD   30-MAY-1996.
XX
PF   06-NOV-1995;   95WO-US014345.
XX
PR   22-NOV-1994;   94US-00343714.
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PA   (USSH) US DEPT HEALTH & HUMAN SERVICES.
XX
PI   Pollard HB, Jacobson KA;
XX
DR   WPI; 1996-268533/27.
DR   N-PSDB; AAT30714.
XX
PT   New CFTR polypeptide(s) - used for identifying CFTR-binding cpds. partic.
PT   novel xanthine derivs., which can be used to treat cystic fibrosis.
XX
PS   Claim 1; Page 44; 61pp; English.
XX
CC   This polypeptide comprises a portion of the cystic fibrosis transmembrane
CC   regulator (CFTR) protein and may be used to identify CFTR binding
CC   compounds and compounds that can activate an impaired chlorine
CC   conductance channel in cells having a reduced apical chlorine
CC   conductance, such as cystic fibrosis. The compounds identified can also
CC   be used for treating other chronic obstructive pulmonary diseases. The
CC   polypeptide spans amino acids 500-530 of the CFTR protein
XX
SQ   Sequence 32 AA;

  Query Match   100.0%; Score 37; DB 2; Length 32;
  Best Local Similarity 100.0%; Pred. No. 1.9;
  Matches   7; Conservative   0; Mismatches   0; Indels   0; Gaps   0;

Qy   1 EYRYRSV 7
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Db   15 EYRYRSV 21

RESULT 15
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ID   AAR13296 standard; protein; 541 AA.
XX
AC   AAR13296;
XX
DT   14-OCT-1991 (first entry)
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DE   CFTR G542X.
XX
KW   Deletion; mutant; diagnosis; antibodies; drug therapy.
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OS   Homo sapiens.
XX
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PN   WO9110734-A.
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PD   25-JUL-1991.
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PF   12-JAN-1990;   90CA-02007699.
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PR   12-JAN-1990;   90CA-02007699.
PR   01-MAR-1990;   90CA-02011253.
PR   10-JUL-1990;   90CA-02020817.
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PA   (HSCR-) HSC RES DEV CORP.
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PI   Tsui LC,  Rommens JM,  Kerem B;
XX
DR   WPI; 1991-238022/32.
DR   N-PSDB; AAQ13059.
XX
PT   Mutant cystic fibrosis trans-membrane conductance regulator gene - used
PT   for producing prods. for diagnosis, screening and therapy of cystic
PT   fibrosis.
XX
PS   Claim 20; Page 124; 178pp; English.
XX
CC   In the G542X mutation Gly (GGA) is changed into a stop codon, resulting
CC   in a shortened polypeptide significantly different from the single amino
CC   acid deletions or alterations. The mutant CF gene when expressed in cells
CC   of the human body, is associated with altered cell function which
CC   correlates with the genetic disease cystic fibrosis. See also AAQ13053-72
XX
SQ   Sequence 541 AA;

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Qy          1 EYRYRSV 7
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Db        514 EYRYRSV 520
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SUMMARIES

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3	37	100.0	32	2	US-08-343-714-4	Sequence 4, Appli
4	37	100.0	32	3	US-09-114-537-4	Sequence 4, Appli
5	37	100.0	150	4	US-09-647-140B-25	Sequence 25, Appl
6	37	100.0	309	1	US-08-463-092B-8	Sequence 8, Appli
7	37	100.0	309	2	US-08-460-907B-8	Sequence 8, Appli
8	37	100.0	836	1	US-08-216-971-2	Sequence 2, Appli
9	37	100.0	836	2	US-08-812-979-2	Sequence 2, Appli
10	37	100.0	1476	3	US-09-256-703-2	Sequence 2, Appli
11	37	100.0	1479	2	US-08-951-912-4	Sequence 4, Appli
12	37	100.0	1479	3	US-09-174-077-4	Sequence 4, Appli
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14	37	100.0	1480	1	US-08-136-742A-2	Sequence 2, Appli
15	37	100.0	1480	1	US-08-135-809A-2	Sequence 2, Appli
16	37	100.0	1480	1	US-08-466-886-17	Sequence 17, Appl
17	37	100.0	1480	2	US-08-951-912-2	Sequence 2, Appli
18	37	100.0	1480	2	US-08-951-912-6	Sequence 6, Appli
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21	37	100.0	1480	2	US-08-691-605-2	Sequence 2, Appli
22	37	100.0	1480	2	US-08-455-552A-14	Sequence 14, Appl
23	37	100.0	1480	3	US-07-890-609-2	Sequence 2, Appli
24	37	100.0	1480	3	US-07-890-609-4	Sequence 4, Appli
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40	37	100.0	1480	4	US-09-425-453A-20	Sequence 20, Appl
41	37	100.0	1480	4	US-08-469-630-17	Sequence 17, Appl
42	37	100.0	1480	4	US-09-949-016-5949	Sequence 5949, Ap
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44	37	100.0	1480	5	PCT-US93-11667-2	Sequence 2, Appli
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RESULT 8
US-08-216-971-2
; Sequence 2, Application US/08216971
; Patent No. 5639661
; GENERAL INFORMATION:
; APPLICANT: Welsh, Michael J.
; APPLICANT: Sheppard, David N.
; TITLE OF INVENTION: NOVEL GENES AND PROTEINS FOR TREATING
; TITLE OF INVENTION: CYSTIC FIBROSIS
; NUMBER OF SEQUENCES: 2
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: LAHIVE & COCKFIELD
; STREET: 60 State Street, suite #510
; CITY: Boston
; STATE: Massachusetts
; COUNTRY: USA
; ZIP: 02109-1875
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk

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;       COMPUTER:  IBM PC compatible
;       OPERATING SYSTEM:  PC-DOS/MS-DOS
;       SOFTWARE:  PatentIn Release #1.0, Version #1.25
;     CURRENT APPLICATION DATA:
;       APPLICATION NUMBER:  US/08/216,971
;       FILING DATE:  23-MAR-1994
;       CLASSIFICATION:  514
;     ATTORNEY/AGENT INFORMATION:
;       NAME:  Arnold, Beth E.
;       REGISTRATION NUMBER:  35,430
;       REFERENCE/DOCKET NUMBER:  UIZ-011
;     TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  (617) 227-7400
;       TELEFAX:  (617) 227-5941
;   INFORMATION FOR SEQ ID NO:  2:
;     SEQUENCE CHARACTERISTICS:
;       LENGTH:  836 amino acids
;       TYPE:  amino acid
;       TOPOLOGY:  linear
;     MOLECULE TYPE:  protein
US-08-216-971-2

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Qy          1 EYRYRSV 7
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Db        514 EYRYRSV 520


RESULT 9
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; Sequence 2, Application US/08812979
; Patent No. 5958893
;  GENERAL INFORMATION:
;    APPLICANT:  Welsh, Michael J.
;    APPLICANT:  Sheppard, David N.
;    TITLE OF INVENTION:  NOVEL GENES AND PROTEINS FOR TREATING
;    TITLE OF INVENTION:  CYSTIC FIBROSIS
;    NUMBER OF SEQUENCES:  2
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  LAHIVE & COCKFIELD
;      STREET:  60 State Street, suite #510
;      CITY:  Boston
;      STATE:  Massachusetts
;      COUNTRY:  USA
;      ZIP:  02109-1875
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/812,979
;      FILING DATE:
;      CLASSIFICATION:
;    PRIOR APPLICATION DATA:
;      APPLICATION NUMBER:  08/216,971
;      FILING DATE:
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Arnold, Beth E.
;      REGISTRATION NUMBER:  35,430
;      REFERENCE/DOCKET NUMBER:  UIZ-011
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (617) 227-7400
;      TELEFAX:  (617) 227-5941
;  INFORMATION FOR SEQ ID NO:  2:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  836 amino acids
;      TYPE:  amino acid
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;      TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
US-08-812-979-2

  Query Match             100.0%;  Score 37;  DB 2;  Length 836;
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SEQ ID NO: 3

SUMMARIES

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6	33	100.0	1014	4	ABB58170	Abb58170 Drosophil
7	33	100.0	1091	2	AAR13303	Aar13303 CFTR Y109
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25	33	100.0	1480	2	AAR13235	Aar13235 CFTR A455
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DT   25-MAR-2003  (revised)
DT   02-MAY-1996  (first entry)
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DE   Truncated cystic fibrosis transmembrane conductance regulator.
XX
KW   Cystic fibrosis; transmembrane conductance; N-terminal; soluble;
KW   truncated; chloride ion channel; gene therapy; CFTR; regulator;
KW   epithelial cells; anion; recombinant production.
XX
OS   Homo sapiens.
XX
PN   WO9525796-A1.
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PD   28-SEP-1995.
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PF   23-MAR-1995;   95WO-US003680.
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PR   23-MAR-1994;   94US-00216971.
XX
PA   (IOWA ) UNIV IOWA STATE RES FOUND INC.
XX
PI   Welsh MJ,  Sheppard DM;
XX
DR   WPI; 1995-344617/44.
DR   N-PSDB; AAT04005.
XX
PT   New truncated CFTR polypeptide - functions as a regulated epithelial cell
PT   anion channel, used for treating cystic fibrosis.
XX
PS   Claim 17; Page 70-73; 85pp; English.
XX
CC   AAT04005 encodes AAR79835 a truncated N-terminal portion of the cystic
CC   fibrosis transmembrane conductance regulator (CFTR), which can be used to
CC   regulate the opening and closing of epithelial cell anion (chloride ion)
CC   channels. The truncated cDNA is useful in CF gene therapy, as it is more
CC   readily accommodated by available gene therapy vectors, and more easily
CC   expressed than full length CFTR. The expressed truncated CFTR protein may
CC   be more soluble and therefore more readily purified from host cells,
CC   useful in the recombinant prodn. of CFTR. (Updated on 25-MAR-2003 to
CC   correct PI field.)
XX
SQ   Sequence 836 AA;

  Query Match             100.0%;  Score 33;  DB 2;  Length 836;
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Qy          1 GQRARIS 7
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Db        551 GQRARIS 557


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AC   AAR13303;
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DT   14-OCT-1991  (first entry)
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DE   CFTR Y1092X.
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KW   Deletion; mutant; diagnosis; antibodies; drug therapy.
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OS   Homo sapiens.
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PF   12-JAN-1990;   90CA-02007699.
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PR   12-JAN-1990;   90CA-02007699.
PR   01-MAR-1990;   90CA-02011253.
PR   10-JUL-1990;   90CA-02020817.
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PA   (HSCR-) HSC RES DEV CORP.
XX
PI   Tsui LC,  Rommens JM,  Kerem B;
XX
DR   WPI; 1991-238022/32.
DR   N-PSDB; AAQ13066.
XX
PT   Mutant cystic fibrosis trans-membrane conductance regulator gene - used
PT   for producing prods. for diagnosis, screening and therapy of cystic
PT   fibrosis.
XX
PS   Claim 20; Page 124; 178pp; English.
XX
CC   In the LY1092X mutation a C to A change is detected at nucleotide
CC   position 3408. This would result in protein synthesis termination at
CC   amino position 1092. Hence the amino acid Tyr is not present in the
CC   truncated polypeptide. The mutant CF gene when expressed in cells of the
CC   human body, is associated with altered cell function which correlates
CC   with the genetic disease cystic fibrosis. See also AAQ13053-72
XX
SQ   Sequence 1091 AA;

  Query Match             100.0%;  Score 33;  DB 2;  Length 1091;
  Best Local Similarity   100.0%;  Pred. No. 2.1e+02;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 GQRARIS 7
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Db        551 GQRARIS 557


RESULT 8
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ID   AAR13308 standard; protein; 1190 AA.
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AC   AAR13308;
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DT   14-OCT-1991  (first entry)
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DE   CFTR 3659 del C.
XX
KW   Deletion; mutant; diagnosis; antibodies; drug therapy.
XX
OS   Homo sapiens.
XX
FH   Key             Location/Qualifiers
FT   Modified-site   50
FT                   /label= phosphorylation_site
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FT   Domain          308. .328
FT                   /label= membrane-spanning_domain
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FT   Domain          433. .584
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PD   25-JUL-1991.
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PF   12-JAN-1990;   90CA-02007699.
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PR   12-JAN-1990;   90CA-02007699.
PR   01-MAR-1990;   90CA-02011253.
PR   10-JUL-1990;   90CA-02020817.
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PA   (HSCR-) HSC RES DEV CORP.
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PI   Tsui LC,  Rommens JM,  Kerem B;
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DR   WPI; 1991-238022/32.
DR   N-PSDB; AAQ13072.
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PT   Mutant cystic fibrosis trans-membrane conductance regulator gene - used
PT   for producing prods. for diagnosis, screening and therapy of cystic
PT   fibrosis.
XX
PS   Claim 20; Page 124; 178pp; English.
XX
CC   3659 del C is a frameshift mutation in exon 19. The 3659 del C mutation
CC   results in a shortened polypeptide significantly different from the
CC   single amino acid deletions or alterations. The mutant CF gene when
CC   expressed in cells of the human body, is associated with altered cell
CC   function which correlates with the genetic disease cystic fibrosis. See
CC   also AAQ13053-72
XX
SQ   Sequence 1190 AA;

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Db 551 GQRARIS 557

SUMMARIES

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2	33	100.0	110	3	US-08-469-617-18	Sequence 18, Appl
3	33	100.0	110	4	US-08-469-630-18	Sequence 18, Appl
4	33	100.0	150	4	US-09-647-140B-25	Sequence 25, Appl
5	33	100.0	309	1	US-08-463-092B-8	Sequence 8, Appli
6	33	100.0	309	2	US-08-460-907B-8	Sequence 8, Appli
7	33	100.0	836	1	US-08-216-971-2	Sequence 2, Appli
8	33	100.0	836	2	US-08-812-979-2	Sequence 2, Appli
9	33	100.0	1476	3	US-09-256-703-2	Sequence 2, Appli
10	33	100.0	1479	2	US-08-951-912-4	Sequence 4, Appli
11	33	100.0	1479	3	US-09-174-077-4	Sequence 4, Appli
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13	33	100.0	1480	1	US-08-136-742A-2	Sequence 2, Appli
14	33	100.0	1480	1	US-08-135-809A-2	Sequence 2, Appli
15	33	100.0	1480	1	US-08-466-886-17	Sequence 17, Appl
16	33	100.0	1480	2	US-08-951-912-2	Sequence 2, Appli
17	33	100.0	1480	2	US-08-469-461-2	Sequence 2, Appli
18	33	100.0	1480	2	US-08-469-461-4	Sequence 4, Appli
19	33	100.0	1480	2	US-08-691-605-2	Sequence 2, Appli
20	33	100.0	1480	2	US-08-455-552A-14	Sequence 14, Appl
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22	33	100.0	1480	3	US-07-890-609-4	Sequence 4, Appli
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24	33	100.0	1480	3	US-08-469-617-17	Sequence 17, Appl
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42	30	90.9	258	4	US-09-252-991A-23325	Sequence 23325, A
43	30	90.9	348	4	US-09-270-767-33144	Sequence 33144, A
44	30	90.9	673	4	US-09-248-796A-20413	Sequence 20413, A
45	30	90.9	1480	4	US-09-425-453A-10	Sequence 10, Appl

RESULT 5
US-08-463-092B-8
; Sequence 8, Application US/08463092B
; Patent No. 5766880
; GENERAL INFORMATION:
; APPLICANT: Cole, Susan P.C.
; APPLICANT: Deeley, Roger G.
; TITLE OF INVENTION: ISOLATED NUCLEIC ACID MOLECULES ENCODING
; TITLE OF INVENTION: MULTIDRUG RESISTANCE PROTEINS
; NUMBER OF SEQUENCES: 9
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: PARTEQ RESEARCH & DEVELOPMENT INNOVATIONS
; STREET: Queen's University at Kingston
; CITY: Kingston
; STATE: Ontario
; COUNTRY: CANADA

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;       ZIP:  K7L 3N6
;     COMPUTER READABLE FORM:
;       MEDIUM TYPE:  Floppy disk
;       COMPUTER:  IBM PC compatible
;       OPERATING SYSTEM:  PC-DOS/MS-DOS
;       SOFTWARE:  ASCII text
;     CURRENT APPLICATION DATA:
;       APPLICATION NUMBER:  US/08/463,092B
;       FILING DATE:  05-JUN-1995
;       CLASSIFICATION:  435
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  07/966,923
;       FILING DATE:  27-0CT-1992
;       CLASSIFICATION:  435
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  08/029,340
;       FILING DATE:  8-MAR-1993
;       CLASSIFICATION:  435
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  08/141,893
;       FILING DATE:  26-0CT-1993
;       CLASSIFICATION:  435
;     PRIOR APPLICATION DATA:
;       APPLICATION NUMBER:  08/407,207
;       FILING DATE:  20-MAR-1995
;       CLASSIFICATION:  435
;     ATTORNEY/AGENT INFORMATION:
;       NAME:  Steeg, Carol Miernicki
;       REGISTRATION NUMBER:  39,539
;       REFERENCE/DOCKET NUMBER:  Q1546
;     TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  (613) 545-2342
;       TELEFAX:  (613) 545-6853
;   INFORMATION FOR SEQ ID NO:  8:
;     SEQUENCE CHARACTERISTICS:
;       LENGTH:  309 amino acids
;       TYPE:  amino acid
;       TOPOLOGY:  linear
;     MOLECULE TYPE:  peptide
;     FRAGMENT TYPE:  internal
US-08-463-092B-8

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Qy          1 GQRARIS 7
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Db        111 GQRARIS 117



RESULT 7
US-08-216-971-2
; Sequence 2, Application US/08216971
; Patent No. 5639661
;  GENERAL INFORMATION:
;    APPLICANT:  Welsh, Michael J.
;    APPLICANT:  Sheppard, David N.
;    TITLE OF INVENTION:  NOVEL GENES AND PROTEINS FOR TREATING
;    TITLE OF INVENTION:  CYSTIC FIBROSIS
;    NUMBER OF SEQUENCES:  2
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  LAHIVE & COCKFIELD
;      STREET:  60 State Street, suite #510
;      CITY:  Boston
;      STATE:  Massachusetts
;      COUNTRY:  USA
;      ZIP:  02109-1875
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
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;     CURRENT APPLICATION DATA:
;       APPLICATION NUMBER:  US/08/216,971
;       FILING DATE:  23-MAR-1994
;       CLASSIFICATION:  514
;     ATTORNEY/AGENT INFORMATION:
;       NAME:  Arnold, Beth E.
;       REGISTRATION NUMBER:  35,430
;       REFERENCE/DOCKET NUMBER:  UIZ-011
;     TELECOMMUNICATION INFORMATION:
;       TELEPHONE:  (617) 227-7400
;       TELEFAX:  (617) 227-5941
;   INFORMATION FOR SEQ ID NO:  2:
;     SEQUENCE CHARACTERISTICS:
;       LENGTH:  836 amino acids
;       TYPE:  amino acid
;       TOPOLOGY:  linear
;     MOLECULE TYPE:  protein
US-08-216-971-2

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Qy          1 GQRARIS 7
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SEQ ID NO: 4

SUMMARIES

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6	33	100.0	836	2	AAR79835	Aar79835 Truncated
7	33	100.0	1091	2	AAR13303	Aar13303 CFTR Y109
8	33	100.0	1190	2	AAR13308	Aar13308 CFTR 3659
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26	33	100.0	1480	2	AAR13297	Aar13297 CFTR S549
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28	33	100.0	1480	2	AAR13894	Aar13894 Cystic fi
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ID AAR79835 standard; protein; 836 AA.
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AC AAR79835;
XX
DT 25-MAR-2003 (revised)
DT 02-MAY-1996 (first entry)
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DE Truncated cystic fibrosis transmembrane conductance regulator.
XX
KW Cystic fibrosis; transmembrane conductance; N-terminal; soluble;
KW truncated; chloride ion channel; gene therapy; CFTR; regulator;
KW epithelial cells; anion; recombinant production.
XX
OS Homo sapiens.
XX
PN WO9525796-A1.
XX
PD 28-SEP-1995.
XX
PF 23-MAR-1995; 95WO-US003680.
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PR 23-MAR-1994; 94US-00216971.
XX
PA (IOWA) UNIV IOWA STATE RES FOUND INC.
XX
PI Welsh MJ, Sheppard DM;
XX
DR WPI; 1995-344617/44.
DR N-PSDB; AAT04005.
XX
PT New truncated CFTR polypeptide - functions as a regulated epithelial cell
PT anion channel, used for treating cystic fibrosis.
XX
PS Claim 17; Page 70-73; 85pp; English.
XX
CC AAT04005 encodes AAR79835 a truncated N-terminal portion of the cystic
CC fibrosis transmembrane conductance regulator (CFTR), which can be used to
CC regulate the opening and closing of epithelial cell anion (chloride ion)
CC channels. The truncated cDNA is useful in CF gene therapy, as it is more
CC readily accommodated by available gene therapy vectors, and more easily
CC expressed than full length CFTR. The expressed truncated CFTR protein may
CC be more soluble and therefore more readily purified from host cells,
CC useful in the recombinant prodn. of CFTR. (Updated on 25-MAR-2003 to
CC correct PI field.)
XX
SQ Sequence 836 AA;

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Db        762 QARRRQS 768

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PD   25-JUL-1991.
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PF   12-JAN-1990;   90CA-02007699.
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PR   12-JAN-1990;   90CA-02007699.
PR   01-MAR-1990;   90CA-02011253.
PR   10-JUL-1990;   90CA-02020817.
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PA   (HSCR-) HSC RES DEV CORP.
XX
PI   Tsui LC,  Rommens JM,  Kerem B;
XX
DR   WPI; 1991-238022/32.
DR   N-PSDB; AAQ13066.
XX
PT   Mutant cystic fibrosis trans-membrane conductance regulator gene - used
PT   for producing prods. for diagnosis, screening and therapy of cystic
PT   fibrosis.
XX
PS   Claim 20; Page 124; 178pp; English.
XX
CC   In the LY1092X mutation a C to A change is detected at nucleotide
CC   position 3408. This would result in protein synthesis termination at
CC   amino position 1092. Hence the amino acid Tyr is not present in the
CC   truncated polypeptide. The mutant CF gene when expressed in cells of the
CC   human body, is associated with altered cell function which correlates
CC   with the genetic disease cystic fibrosis. See also AAQ13053-72
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SQ   Sequence 1091 AA;

  Query Match             100.0%;  Score 33;  DB 2;  Length 1091;
  Best Local Similarity   100.0%;  Pred. No. 3.4e+02;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

Qy          1 QARRRQS 7
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Db        762 QARRRQS 768


SUMMARIES

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     4      33   100.0    1479   2  US-08-951-912-4              Sequence 4, Appli
     5      33   100.0    1479   3  US-09-174-077-4              Sequence 4, Appli
     6      33   100.0    1480   1  US-07-637-621-2              Sequence 2, Appli
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9	33	100.0	1480	1	US-08-466-886-17	Sequence 17, Appl
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21	33	100.0	1480	3	US-08-681-838A-3	Sequence 3, Appli
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34	33	100.0	1480	4	US-08-469-630-17	Sequence 17, Appl
35	33	100.0	1480	4	US-09-949-016-5949	Sequence 5949, Ap
36	33	100.0	1480	4	US-09-405-735-2	Sequence 2, Appli
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41	30	90.9	217	4	US-09-252-991A-30509	Sequence 30509, A
42	30	90.9	286	4	US-09-252-991A-22717	Sequence 22717, A
43	30	90.9	314	4	US-09-252-991A-18752	Sequence 18752, A
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RESULT 1
US-08-216-971-2
; Sequence 2, Application US/08216971
; Patent No. 5639661
;  GENERAL INFORMATION:
;    APPLICANT:  Welsh, Michael J.
;    APPLICANT:  Sheppard, David N.
;    TITLE OF INVENTION:  NOVEL GENES AND PROTEINS FOR TREATING
;    TITLE OF INVENTION:  CYSTIC FIBROSIS
;    NUMBER OF SEQUENCES:  2
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  LAHIVE & COCKFIELD
;      STREET:  60 State Street, suite #510
;      CITY:  Boston
;      STATE:  Massachusetts
;      COUNTRY:  USA
;      ZIP:  02109-1875
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/08/216,971
;      FILING DATE:  23-MAR-1994
;      CLASSIFICATION:  514
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  Arnold, Beth E.
;      REGISTRATION NUMBER:  35,430
;      REFERENCE/DOCKET NUMBER:  UIZ-011
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;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  (617) 227-7400
;      TELEFAX:  (617) 227-5941
;  INFORMATION FOR SEQ ID NO:  2:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  836 amino acids
;      TYPE:  amino acid
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
US-08-216-971-2

  Query Match             100.0%;  Score 33;  DB 1;  Length 836;
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Db        762 QARRRQS 768


RESULT 6
US-07-637-621-2
; Sequence 2, Application US/07637621
; Patent No. 5407796
;  GENERAL INFORMATION:
;    APPLICANT:  cutting, gary
;    APPLICANT:  antonarakis, stylianos e
;    APPLICANT:  kazazian jr., haig h
;    TITLE OF INVENTION:  CYSTIC FIBROSIS MUTATION CLUSTER
;    NUMBER OF SEQUENCES:  4
;    CORRESPONDENCE ADDRESS:
;      ADDRESSEE:  Banner, Birch, McKie and Beckett
;      STREET:  1001 G Street, N.W.
;      CITY:  Washington, D.C.
;      COUNTRY:  USA
;      ZIP:  20001
;    COMPUTER READABLE FORM:
;      MEDIUM TYPE:  Floppy disk
;      COMPUTER:  IBM PC compatible
;      OPERATING SYSTEM:  PC-DOS/MS-DOS
;      SOFTWARE:  PatentIn Release #1.0, Version #1.25
;    CURRENT APPLICATION DATA:
;      APPLICATION NUMBER:  US/07/637,621
;      FILING DATE:  19910104
;      CLASSIFICATION:  435
;    ATTORNEY/AGENT INFORMATION:
;      NAME:  kagan, sarah a
;      REGISTRATION NUMBER:  32,141
;      REFERENCE/DOCKET NUMBER:  1107.030010
;    TELECOMMUNICATION INFORMATION:
;      TELEPHONE:  202-508-9100
;      TELEFAX:  202-508-9100
;  INFORMATION FOR SEQ ID NO:  2:
;    SEQUENCE CHARACTERISTICS:
;      LENGTH:  1480 amino acids
;      TYPE:  AMINO ACID
;      TOPOLOGY:  linear
;    MOLECULE TYPE:  protein
;    ORIGINAL SOURCE:
;      ORGANISM:  HOMO SAPIENS
US-07-637-621-2

  Query Match             100.0%;  Score 33;  DB 1;  Length 1480;
  Best Local Similarity   100.0%;  Pred. No. 1.2e+02;
  Matches    7;  Conservative    0;  Mismatches    0;  Indels    0;  Gaps    0;

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Db        762 QARRRQS 768
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